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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Maura C. Cannon, Francis C. Cannon, Gabriel J. McCool, Henry E. Valentin, and Kenneth J. Gruys

Serial No.: 09/479,040 Art Unit: 1655

Filed: January 7, 2000 Examiner: A. Chakrabarti

For: *"POLYHYDROXYALKANOATE BIOSYNTHESIS ASSOCIATED PROTEINS AND CODING REGION IN BACILLUS MEGATERIUM"*

Assistant Commissioner for Patents
Washington, D.C. 20231

AMENDMENT AND RESPONSE TO OFFICE ACTION

Sir:

Responsive to the Office Action mailed on April 11, 2002, please amend the application as follows.

It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-1868.

See Clean Version

In the Claims

1. (Three Times Amended) An isolated or purified nucleic acid segment comprising a nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein, wherein the nucleic acid sequence is a nucleic acid sequence at least about 80% identical to SEQ ID NO:8 that hybridizes under stringent conditions to SEQ ID NO:8 or the complement thereof, and

encodes a protein at least about 80% identical to SEQ ID NO:9, and

[that] has 3-keto-acyl-CoA reductase activity higher for [for] D-isomers of C6 carbon chains than for C4 carbon chains.

24. (Amended) The nucleic acid segment, vector, or cell of claims 1, [2,]4, 5, or 6, wherein the nucleic acid sequence is SEQ ID NO:8.

Remarks

Claims 1, 3-6, 9, 11-14, 24 and 25 are pending. Claims 1 and 24 have been amended to remove typographical errors. The Examiner stated in a phone interview with the Applicants representative (May 16, 2002) that the rejection of claims under 35 U.S.C. §101, as stated in the Office Action mailed on April 11, 2002, was in error and should be disregarded.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1, 3-6, 9, 11-14, and 24-25 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Examiner asserts that the disclosed species are not representative of the highly variant nucleic acid genus. However, as will be discussed, the genus is limited base upon the common features dictated, in part, by the "target" hybridization partner, SEQ ID NO:8. The claimed nucleic acids depend upon hybridization interactions which are dependent upon hydrogen bonding. Therefore, in order for the claimed nucleic acid to hybridize to SEQ ID

NO:8, under any set of conditions (and in particular, stringent conditions), one of ordinary skill in the art will confirm that hydrogen bond donor and acceptor sites have to be in the correct spatial location, orientation, and have the correct charge. These bonding patterns drive the non-covalent interactions between bases of nucleic acid (whether intra- or inter-molecular – i.e. single strand or double strand) and are an inherent part of any nucleic acid. One of skill in the art would realize that it is this arrangement in SEQ ID NO:8 that defines the structure of the claimed nucleic acid. Hybridizing nucleic acids are limited and defined by the sequence of the SEQ ID NO:8 target nucleic acid molecule. Given the minor and major groove sequences of the sequence to be targeted (SEQ ID NO:8), the arrangement of possible hydrogen bonds to be utilized by the hybridizing nucleic acid is defined, therefore limiting the structure of the claimed nucleic acid.

As stated in M.P.E.P. § 2173.05(t), which describes the standard to be applied to compounds and compositions, "a compound of unknown structure may be claimed by a combination of physical and chemical characteristics." See *Ex parte Brian*, 118 USPQ 242 (Bd. App. 1958). M.P.E.P. § 2173.05(t) further states that "a compound may also be claimed in terms of the process by which it is made without raising an issue of indefiniteness." It is important to note that only *after* obtaining the correct target nucleic acid sequence (which the applicants have – SEQ ID NO:8), can the claimed compound and its structure be elucidated. This is routine to those skilled in the art. The structural features common to the members of the claimed genus can only be determined once the hydrogen bonding arrangement of the target sequence is derived. Once the target nucleic acid sequence is derived, the major and minor groove structures can be

easily inserted into any number of commercially available computer programs and the structural features of the claimed nucleic acid be determined. The structure of the claimed nucleic acid is clearly limited based on the requirement for it to hybridize to SEQ ID NO:8.

The "hybridizing" nature of the claimed nucleic acid molecule, in combination with the specific activity of the encoded protein, distinguishes the claimed nucleic acid from others. Nucleic acids that form duplexes *via* hybridization do not necessarily have the requisite correct charge and spatial orientation of the potential hydrogen bond donors and acceptors to be specific for presentation and binding to SEQ ID NO:8. While most, if not all, hybridizing nucleic acids do have hydrogen bonding sites, only a few will have the necessary pattern of sites to be utilized specifically by the SEQ ID NO:8 nucleic acid. The identification of SEQ ID NO:8 "target" is required for the determination of the structure of any nucleic acid sequence that hybridizes to the sequence "target". Therefore the structural features common to the claimed nucleic acid molecule, as defined by the term "hybridizes under stringent conditions", the requisite hydrogen bonding acceptor and donor sites harbored by SEQ ID NO:8, and a protein harboring the claimed specific activity, are clearly described.

The applicant respectfully reminds the Examiner that the inquiry into adequate written description is not performed in a vacuum. "Knowledge of one skilled in the art is relevant to meeting [the written description] requirement." *Enzo Biochem, Inc. v. Gen-Probe*, Docket No. 01-1230 (Fed. Cir. Apr. 2, 2002) (slip op.). This fact has implications not only for validity challenges, but also for patent prosecution. *See In re Alton*, 76 F.3d 1168, 1174-75 (Fed. Cir. 1996).

Based upon the foregoing discussion, the skilled artisan can envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, without having to delve into the "complexity or simplicity of the method of isolation".

Claims 1, 3-6, 9, and 11-14 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Examiner asserts that there is no disclosure of common elements of the claimed sequences, nor is there any teaching of structural limitations which provide guidance for identifying such sequences. As noted in the foregoing discussion, SEQ ID NO:8 limits and defines the claimed nucleic acid sequences structurally. Furthermore, the claimed nucleic acid encodes a protein harboring specific reductase activity for D-isomers of C6 carbon chains. One of ordinary skill in the art will realize that this enzymatic activity relies upon the three-dimensional structure of the encoded protein, which is ultimately dictated by the nucleic acid sequence. The specific reductase activity sheds additional light onto the already defined structure of the claimed nucleic acids. The information encoded in the nucleic acid is expressed indirectly *via* other molecules: DNA directs the synthesis of specific RNA and protein molecules. What is presented here is a two-pronged approach to defining and characterizing the claimed nucleic acids. The first approach structurally defines the claimed nucleic acid in terms

of the "target" SEQ ID NO:8. As described above, SEQ ID NO:8 nucleic acid bases provide hydrogen bonding arrangements and hydrophobic interactions that are known to one of ordinary skill in the art. These "forces" define the structure of SEQ ID NO:8 in a way that provides one with a mental picture of a defined "space" that can only be accessed (or hybridized to) by a nucleic acid of the correct "shape". It will help, perhaps, to view SEQ ID NO:8 as a "lock" and the claimed nucleic acid as the "key", wherein the shape of the interior of the lock is defined by hydrophobic, hydrogen bonding, and electrostatic forces provided by nucleic acid bases of SEQ ID NO:8. The key (claimed nucleic acid) will only fit into the lock if it is able to "complement" these forces and hybridize to the target.

The second approach corresponds to structurally defining the claimed nucleic acid in terms of the encoded protein, or reductase. One of ordinary skill in the art will readily agree that the chemical and physical properties of the reductase, which specifically recognizes the D-isomer of C6 carbon chains as substrate, are predicated by amino acid sequence and, ultimately, by the nucleic acid sequence governing amino acid identity. In other words, the reductase is structurally defined by the nucleic acid sequence (at least 80% homologous to SEQ ID NO:8). The converse of this is also true: the identity of the amino acid sequence and, ultimately, the three-dimensional structure of the reductase (as defined by the activity) defines the nucleic acid sequence. The specification did not label just any sequence with the term "reductase". The amino acid sequence harboring at least 80% identity to SEQ ID NO:9 *is* the protein that harbors a C6 carbon chain specific activity. This activity is readily assayed using methods common in

the art and described at page 60 and Table 6. The claimed nucleic acid encodes, and is structurally determined by, the reductase and its activity.

SUMMARY UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

An understanding of nucleic acid structure is the result of a detailed analysis of the molecular interactions between nucleic acids (i.e. the hydrogen bonding arrangements and hydrophobic interactions). One of skill in the art will recognize that, in view of the present specification, the identification and isolation of the SEQ ID NO:8 sequence dictates and defines the specific conformation and the "order" of "complementary" groups on the claimed nucleic acid that must be assembled in order to recognize and hybridize to the SEQ ID NO:8 under high stringency conditions.

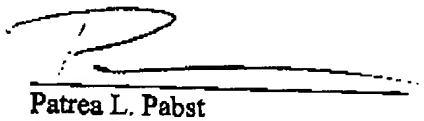
Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1 and 3-6 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The term "for" has been deleted from claim 1, thereby clarifying "D-isomer". Claim 24 has been amended to depend from claims 1, 4, 5, or 6, thereby deleting reference to the non-elected claim 2.

Allowance of claims 1, 3-6, 9, 11-14, 24 and 25 is respectfully solicited.

Respectfully submitted,



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